亞盛醫藥
Ascentage Pharma

ASCENTAGE PHARMA GROUP INTERNATIONAL
亞盛醫藥集團
(Incorporated in the Cayman Islands with limited liability)
(Stock Code: 6855)

Voluntary Announcement

Ascentage Pharma Announces IND Clearance by the US FDA for APG-2575 as Single Agent or in Combinations for the Treatment of ER+ Breast Cancer and Other Solid Tumors

Ascentage Pharma Group International (the "**Company**" or "**Ascentage Pharma**") is pleased to announce that the Investigational New Drug (IND) application for the company's novel Bcl-2 inhibitor, APG-2575, has been cleared by the US Food and Drug Administration (FDA) and the company is poised to initiate a clinical study of APG-2575 as a single agent or in combination with other antitumor therapies for the treatment of patients with advanced estrogen receptor-positive (ER+) breast cancer or other solid tumors.

This global multicenter, open-label Phase Ib/II clinical study is designed to evaluate the safety, tolerability, pharmacokinetics (PK), and preliminary efficacy of APG-2575 as a single agent in patients with advanced solid tumors, or in combination with cyclin-dependent kinase 4/6 (CDK4/6) inhibitor palbociclib in patients with metastatic ER+ and human epidermal growth factor receptor 2-negative (ER+/HER2-) breast cancer relapsed or refractory to prior treatment with CDK4/6 inhibitors.

Breast cancer is one of the most common malignancies in women. About 75% of all breast cancer cases are hormone receptor positive (HR+)[1], mainly estrogen receptor positive (ER+), and the antiapoptotic protein Bcl-2 is overexpressed in around 85% of this subset[2]. Endocrine therapy is the standard of care treatment for patients with early-stage or metastatic HR+/HER2- breast cancer. In the first-line treatment of metastatic ER+ breast cancer, a CDK4/6 inhibitor (including palbociclib, ribociclib, and abemaciclib) in combination with endocrine therapy to target the CCND1-CDK4/6-RB pathway can offer longer progression-

free survival (PFS) and overall survival (OS), as compared to endocrine therapy alone[3,4]. In the second-line treatment, phosphoinositide 3-kinase (PI3K) inhibitor plus fulvestrant and everolimus plus endocrine therapy can effectively target the PI3K-AKT-mTOR pathway, thus offering additional treatment options for patients who failed first-line treatments[3]. However, patients treated with endocrine therapies and targeted therapies commonly develop drug resistances, eventually necessitating chemotherapies. Therefore, there is an urgent clinical need for novel targeted therapies that can effectively blockade mutational pathways and delay chemotherapies.

About APG-2575

APG-2575 is a novel, orally administered small-molecule Bcl-2–selective inhibitor being developed by Ascentage Pharma. APG-2575 is designed to treat hematologic malignancies and solid tumors by selectively blocking antiapoptotic protein Bcl-2 to restore the normal apoptosis process in cancer cells. APG-2575 is the first China-developed Bcl-2 inhibitor entering clinical development in China. Thus far, APG-2575 has received clearances and approvals for multiple Phase Ib/II clinical studies in China, the US, Australia and Europe, and is currently being developed in a range of hematologic malignancies globally. As a single agent, APG-2575 has potent antitumor activity in Bcl-2-dependent tumor cell lines, and has shown broad antitumor effects when combined with other antitumor therapies.

Previously, preclinical data of APG-2575 in combination with palbociclib showed that palbociclib can induce cell cycle arrest and apoptosis, while APG-2575 can bolster the expression of proapoptotic proteins such as BIM and downregulate ER levels, while lowering the levels of phosphorylated Rb protein, and the protein level of cyclin D1 and E. Therefore, Bcl-2 inhibitors combined with CDK4/6 inhibitors can synergistically enhance cell cycle arrest while inducing the cell death of ER+ breast cancer cells.

About Ascentage Pharma

Ascentage Pharma is a China-based, globally focused, clinical-stage biotechnology company engaged in developing novel therapies for cancers, CHB (Chronic hepatitis B), and age-related diseases. On October 28, 2019, Ascentage Pharma became listed on the Main Board of The Stock Exchange of Hong Kong Limited with the stock code: 6855.HK.

Ascentage Pharma has its own platform for developing therapeutics that inhibit protein-protein interactions to restore apoptosis or programmed cell death. The company has built a pipeline of eight type I small molecule clinical drug candidates which have entered the clinical development stage, including novel, highly potent Bcl-2 inhibitors, as well as candidates aimed at IAP and MDM2-p53 pathways, and next-generation tyrosine kinase inhibitors (TKIs). Ascentage Pharma is also the only company in the world with active

clinical programs targeting all key apoptosis regulators. The Company is conducting more than 40 Phase I/II clinical trials in China, the US and Australia. HQP1351, the Company's core drug candidate developed for the treatment of drug-resistant chronic myeloid leukemia (CML), has been granted an Orphan Drug Designation (ODD) and a Fast Track Designation (FTD) by the US FDA, and a New Drug Application (NDA) for the drug candidate has been submitted and subsequently granted Priority Review by the Center for Drug Evaluation (CDE) in China. As at the date of this announcement, Ascentage Pharma has obtained a total of eleven ODDs from the US FDA for four of the Company's investigational drug candidates.

Cautionary Statement required by Rule 18A.05 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited: We cannot guarantee that we will be able to obtain further approval for, or ultimately market, HQP1351 and APG-2575 successfully.

By order of the Board
Ascentage Pharma Group International
Dr. Yang Dajun
Chairman and Executive Director

Suzhou, People's Republic of China, June 15, 2021

As at the date of this announcement, the Board of Directors of the Company comprises Dr. Yang Dajun as Chairman and executive Director, Dr. Wang Shaomeng, Dr. Tian Yuan, Dr. Lu Simon Dazhong and Mr. Liu Qian as non-executive Directors, and Mr. Ye Changqing, Dr. Yin Zheng, Mr. Ren Wei and Dr. David Sidransky as independent non-executive Directors.

References:

1. McDonald, E.S., et al., Clinical Diagnosis and Management of Breast Cancer. J Nucl Med, 2016. 57 Suppl 1: p. 9s-16s.

2. Razavi, P., et al., The Genomic Landscape of Endocrine-Resistant Advanced Breast Cancers. Cancer Cell, 2018. 34(3): p. 427-438.e6.

3. Rozeboom, B., N. Dey, and P. De, ER+ metastatic breast cancer: past, present, and a prescription for an apoptosis-targeted future. Am J Cancer Res, 2019. 9(12): p. 2821-2831.

4. Lynce, F., A.N. Shajahan-Haq, and S.M. Swain, CDK4/6 inhibitors in breast cancer therapy: Current practice and future opportunities. Pharmacol Ther, 2018. 191: p. 65-73.